

### DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 13, 2010, has been entered.

2. Claims 1-4, 6, and 9-74 have been cancelled.

Claims 75-79 have been newly added and are drawn to the elected invention.

Claims 5, 7, 8, and 75-79 are pending and are examined in the present office action.

### ***Rejections and Objections that are Withdrawn***

3. All objections and rejections of claims 72 and 73 are withdrawn in light of the Applicant's cancellation of these claims.

4. The rejection of claims 5, 7, and 8 under 35 U.S.C. 103 as being unpatentable over Howard et al, in view of Bliel et al, and further in view of Russell-Jones, G.J is withdrawn in light of the Applicant's amendments to the claims.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 5, 8, 75, 77, and 79 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. All dependent claims are included in these rejections.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can

render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claims 5, 75, and 77 recite the broad recitation “comprising an antigen or antibody, and further comprising a mucosal targeting protein”, and the claims also recite “comprising ZP3 and *E. coli* enterotoxin subunit B” which is the narrower statement of the range/limitation.

In addition, the claims construction includes the recitation “further comprising” which is confusing, because it appears that the claim is encompassing a homogenate of a plant expressing ZP3 and *E. coli* enterotoxin subunit B in addition to expressing an antigen or antibody and a mucosal targeting protein. It is not clear to the Examiner if the Applicant intends to be claiming a homogenate of a plant expressing ZP3 and *E. coli* enterotoxin subunit B in addition to expressing an antigen or antibody and a mucosal targeting protein, or if the Applicant intends to be claiming a homogenate of a plant expressing ZP3 and *E. coli* enterotoxin subunit B or if the Applicant intends to be claiming a homogenate of a plant expressing an antigen or antibody and a mucosal targeting protein.

6. Claims 5, 75, and 77 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims encompass a homogenate of a plant “expressing a heterologous contraceptive protein comprising ZP3 and *E. coli* enterotoxin subunit B, further comprising an antigen or antibody, and further comprising a mucosal targeting protein”. As discussed above in the rejection under 35 USC 112, 2<sup>nd</sup> paragraph, one interpretation of this recitation is that the claims are directed to a homogenate of a plant expressing ZP3 and *E. coli* enterotoxin subunit B in addition to expressing an antigen or antibody and a mucosal targeting protein. The Examiner can not find support in the originally filed specification for co-expression of ZP3 and an additional antigen or antibody and *E. coli* enterotoxin subunit B and an additional mucosal targeting protein. Therefore, this recitation introduces **NEW MATTER**. The Applicant is advised to amend the claims to remove the new matter.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at

the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 5, 7, 8, and 75-79 are rejected under 35 U.S.C. 103(a) as being unpatentable over Howard et al (WO 97/10347; published on Mar. 20, 1997), in view of Bliel et al (WO 98/00440; published on Jan. 8, 1998), further in view of Russell-Jones, G.J. (J. of Controlled Release (2000) Vol. 65; pp. 49-54), and further in view of Mowat et al (Immunology Letters (1999) Vol. 65; pp. 133-140). The Applicant's arguments in the response filed on April 13, 2010, were fully considered but were not found to be persuasive.

The claims are drawn to a stable dry homogenate of a transgenic plant expressing a heterologous contraceptive protein comprising ZP3 and *E. coli* enterotoxin subunit B by plant chromosomal expression in the absence of a viral intermediate, further comprising an antigen or antibody, and further comprising a mucosal targeting protein, in combination with a saponin adjuvant, that induces an immune response to said contraceptive protein in an animal upon administration to the animal, including wherein the homogenate is mixed with a pharmaceutically acceptable carrier.

It is noted that claims 77 and 78 include the recitation "wherein said homogenate is administered more than five times to said animal", however, the claims are product claims rather than method claims, therefore this is an intended

use of the claimed product, and it does not limit the product, itself. Therefore, this recitation is not given weight for searching for prior art.

Howard et al teach the production of vaccines in transgenic plants (see entire document), and specifically the production of a vaccine against transmissible gastroenteritis virus (TGEV) (see claim 2). They specifically teach oral administration of plant seed and the use of the transgenic plant seed as a feed composition (see abstract). They teach that transgenic plants, plant organs, and seeds can be combined into animal feed using methods and feed components known to those of skill in the art (see last sentence on page 9), and this combining would yield a homogenate. They specifically claim feed and an immunogenic composition comprising the recombinant antigen (see claims 22 and 23). They specifically teach that when plants have set seed they are placed in a holding area to mature and dry down (which is a dehydrating step) (see paragraph bridging pages 13-14). They claim a composition that further comprises an adjuvant (see claim 24); and adjuvants are pharmaceutically acceptable carriers. Howard et al teach agrobacterium-mediated transformation (see page 19, last paragraph), and this introduces the transgene into the plant chromosome for chromosomal expression with no viral intermediate.

Howard et al do not teach an immunocontraceptive protein, nor do they teach a mucosal targeting protein, nor do they teach saponin adjuvant.

Bleil et al teach immunocontraceptive vaccines that are orally administered in bait or feed formulations (see abstract). These feed formulations are pharmaceutically acceptable carriers. Immunocontraceptives work because the subject generates antibodies against the contraceptive protein (see pages 1-2). Bleil et al specifically teach ZP3 from mouse sperm (see first paragraph on page 3), and this is specie's specific for mice.

Russell-Jones teaches mucosal binding proteins as carriers for oral vaccine delivery (see right column on page 51). Russell-Jones also provides a general review of oral vaccine delivery, and specifically mentions the oral contraceptive protein ZP3 (see right column on page 52).

Muwat et al teach the saponin adjuvant Quil A for use with orally-administered vaccines (see abstract).

At the time the invention was made, it would have been obvious and within the scope of one of ordinary skill in the art to modify the transgenic plants taught by Howard et al to express an immunocontraceptive, such as those taught by Bleil et al. One would have been motivated to do so because Bleil et al teach that oral contraceptive vaccines are cost effective and lack side effects (see page 1). Given that Howard et al present their method as a method that is generally applicable to the production of any vaccine, and given the successes taught by Howard et al in producing a TGEV vaccine in transgenic plants, one would have had an expectation of success in producing a transgenic edible vaccine in plant tissue that could be

administered as a dry homogenate in animal feed. Given the teachings of Russell-Jones that utilizing a mucosal binding protein with vaccine candidates was successful and provided a good antibody response (see right column on page 51), one would have been motivated to utilize a mucosal binding protein as a carrier for an oral vaccine and one would have expected this mucosal binding protein to increase the immune response to the orally-delivered vaccine. Given the success of achieving immunocontraception with several different oral contraceptive vaccines as taught by Bleil et al (see page 1); one would have had a reasonable expectation of success in producing transgenic plants expressing a recombinant immunocontraceptive protein.

At the time the invention was made, it would have been obvious and within the scope of one of ordinary skill in the art to utilize the saponin adjuvant taught by Muwat et al. One would have been motivated to utilize a lipophilic immune stimulating complex containing saponin (referred to as ISCOMS), because Muwat et al teach that the immune response to a model vaccine was significantly elevated when the saponin-containing adjuvant was utilized (see Figure 1 and Discussion on page 136).

#### APPLICANT'S ARGUMENTS

The Applicant argues that the Examiner has not established a prima facie case of obviousness which requires a suggestion or motivation to combine the reference teachings, a reasonable expectation of success, and the references must

teach or suggest all the claim limitations. This is not persuasive, however, because the Examiner has provided motivation to combine the references, excerpts from the rejection are shown here:

- “One would have been motivated to do so because Bleil et al teach that oral contraceptive vaccines are cost effective and lack side effects (see page 1)”
- “one would have been motivated to utilize a mucosal binding protein as a carrier for an oral vaccine and one would have expected this mucosal binding protein to increase the immune response to the orally-delivered vaccine”
- “One would have been motivated to utilize a lipophilic immune stimulating complex containing saponin (referred to as ISCOMS), because Muwat et al teach that the immune response to a model vaccine was significantly elevated when the saponin-containing adjuvant was utilized (see Figure 1 and Discussion on page 136).”

This is ample motivation for one of ordinary skill in the art to combine the teachings. However, even if there were no teaching, suggestion, or motivation to combine, *KSR* forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. See the recent Board decision *Ex parte Smith*, - - USPQ2d - - , slip op. at 20, (Bd. Pat. App. & Interf. June

25, 2007) (citing *KSR*, 82 USPQ2d at 1396) (available at <http://www.uspto.gov/web/offices/dcom/bpai/prec/fd071925.pdf>).

The Examiner explained why there would be a reasonable expectation of success: "Given the success of achieving immunocontraception with several different oral contraceptive vaccines as taught by Bleil et al (see page 1); one would have had a reasonable expectation of success in producing transgenic plants expressing a recombinant immunocontraceptive protein."

The Examiner has accounted for every limitation in every claim.

The Applicant argues that Howard et al does not teach or suggest expression by plant chromosomal expression in the absence of a viral intermediate (see first paragraph on page 7 of the response). This is not persuasive, however, because Howard et al teach agrobacterium-mediated transformation (see page 19, last paragraph), and this introduces the transgene into the plant chromosome for chromosomal expression with no viral intermediate. Therefore, this limitation is taught by Howard et al.

The Applicant argues that Howard does not teach a contraceptive protein that is species specific and that none of Bliel, Russell-Jones or Mowat cure this deficiency (see first paragraph on page 7). This is not persuasive, however, because Bliel et al specifically teach ZP3 from mouse sperm (see first paragraph on page 3), and this is specie's specific for mice.

The Applicant argues that the references do not teach administering the homogenate to animals more than five times (see second paragraph on page 7). This is not persuasive, however, because the claims are product claims rather than method claims, therefore this is an intended use of the claimed product, and it does not limit the product, itself. Therefore, this recitation is not given weight for searching for prior art.

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cathy K. Worley whose telephone number is (571) 272-8784. The examiner is on a variable schedule but can normally be reached on M-F 10:00 - 4:00 with additional variable hours before 10:00 and after 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Cathy K. Worley/  
Primary Examiner, Art Unit 1638